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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,505	01/15/2004	Caroline Delattre	1016800-000583.001	6320

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EXAMINER	
FERNANDEZ, SUSAN EMILY	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
11/14/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/757,505	DELATTRE ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-11,13,14,16,17,21,24,25,27-29,43-51 and 61-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-11,13,14,16,17,21,24,25,27-29,43-51 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8-22-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed August 22, 2007, has been received and entered.

Claims 2-8, 12, 15, 18-20, 22, 23, 26, 30-42, and 52-60 are cancelled. Claims 61-66 are new.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 43-51, and 61-66 are pending and examined on the merits to the extent they read on the elected subject matter and species. The species election in the replies filed on February 23, 2005 and February 24, 2006 apply to the amended claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite "at least one compound which stimulates the activity of aspartylglucosaminidase (AGA)" though the specification only indicates sodium dodecyl sulphate (SDS) and sodium lauryl ether sulphate as suitable compounds, and does not describe

any other compounds appropriate for stimulating the activity of AGA. Thus, a holding of lack of written description is clearly required.

Claims 43-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding undue experimentation, *In re Wands*, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) states:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (Citations omitted).

Claims 43-51 indicate that the at least one compound which stimulates the activity of AGA is sodium dodecyl sulfate (SDS) or sodium lauryl ether sulfate. However, it is unclear that either of these two compounds increase the rate of the enzymatic reaction of aspartylglucosaminidase. No working examples are provided in the specification that show that SDS or sodium lauryl ether sulfate increase the activity of AGA. Moreover, Enomaa et al. (Biochem. J. 1992. 286: 613-618) observes the effects of SDS on AGA activity at various temperatures and SDS concentrations (page 613, last paragraph through page 614, first paragraph). Figure 3 on page 614 of Enomaa et al. compares the activity of AGA in the absence or presence of SDS, and it is evident that for every temperature and concentration of SDS tested,

the presence of SDS decreases the activity of AGA. Therefore, the prior art clearly teaches that SDS is not a compound which stimulates the activity of AGA.

Because of the lack of working examples and the state of the prior art, the application is not enabled for SDS or sodium lauryl ether sulfate as compounds which stimulate the activity of aspartylglucosaminidase.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 24, 25, and 27-29 are indefinite since the use of the term "optionally" in the claim does not clearly indicate whether at least one compound which stimulates the activity of AGA is present and a critical element. The metes and bounds of the claims are unclear because of the term. Thus, claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 61-66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fein (US 2003/0026794) in view of Baumann et al. (Biochem. J. 1989. 262: 189-194).

Fein discloses a method "...for treating a patient having a condition involving the epidermal, and/or dermal, and/or subcutaneous layer of skin using a composition containing at least one enzyme that affects one or more particular layers of skin" (page 1, paragraph [0008]). As the methods taught in Fein are for treating hyperkeratotic disorders wherein normal desquamation does not occur, such as xerosis (dry skin) (page 3, paragraphs [0029] and [0034]), a regime or regimen for promoting desquamation of the skin and/or for promoting hydration of the skin is taught, as required by instant claims 1, 24, 27, 61, and 63. Since a regime or regimen for promoting desquamation/hydration of skin is taught, regimen for promoting cicatrisation (instant claims 25 and 64), facilitating the penetration into the skin of a cosmetic/dermatological active agent (instant claims 28 and 65), and combating bacterial adhesion to the skin (instant claims 29 and 66) are also taught. The Fein invention teaches the topical application of enzymes

(abstract), where the enzymes may be amidases or ceramidases (page 3, paragraph [0042]) which are actually recited as hydrolase polypeptides having amidase activity in the pending claims, but were not elected for examination. The enzymes are delivered in a suitable, physiologically acceptable formulation (page 5, paragraph [0053]) in an amount which can range from about $1x10^{-9}$ % w/v to about 80% w/v of the formulation (page 2, paragraph [0010]). Thus, limitations recited in instant claims 1, 9-11, 13, and 14 are taught by the reference.

The enzyme formulation of the Fein invention "...may also contain other compounds that have desirable therapeutic, cosmetic, and/or aesthetic properties, that either do not affect or only minimally affect the activity of the enzyme" (page 5, paragraph [0054]). Alpha-hydroxy acids, EDTA, a moisturizing cream base, and exfoliants (thus permeating agent) may be included in the enzyme formulation (page 5, paragraph [0054]). Therefore, limitations of claims 16 and 17 are taught (EDTA is a desquamating agent).

Fein differs from the claimed invention in that it does not teach that the hydrolase enzyme topically applied to the skin is aspartylglucosaminidase (AGA). Furthermore, Fein does not teach that the enzyme formulation further comprises at least one compound which stimulates the activity of AGA, as required by instant claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, and 43-51.

Baumann et al. discusses human aspartylglucosaminidase (AGA), an enzyme known to hydrolyze beta-aspartylglycosylamine linkages (page 189, first paragraph). For purified AGA, the effect of pH on enzymatic activity was determined with various buffers (page 192, last paragraph through page 193, first paragraph). As Figure 5 on page 193 demonstrates, the

enzyme activity was most optimal at a pH of about 6, where the buffer used at this pH is a citrate/phosphate buffer.

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have used aspartylglucosaminidase as the hydrolase enzyme of the Fein enzyme formulation for treating skin. One of ordinary skill in the art would have been motivated to do this since there would have been a reasonable expectation of success in substituting one hydrolase for another. Furthermore, Fein does not limit which hydrolases may be used in his invention. Note also that Fein teaches topical administration of formulations comprising amidases or ceramidases which are recited as non-elected species in the instant claims.

Additionally, it also would have been obvious to have included a buffer at a pH of about 6, such as a citrate/phosphate buffer, in the Fein enzyme formulation comprising aspartylglucosaminidase (AGA). One of ordinary skill in the art would have been motivated to do this since such a buffer at this pH results in optimal AGA activity, thus ensuring that the AGA is active, which is necessary for the enzyme to act on the skin. Such a buffer at pH of about 6 modifies the environment of the enzyme to one that is favorable to the activation of the enzyme. It is noted that this buffer at pH of about 6 stimulates the activity of AGA compared to buffers at other pHs. Though Fein indicates that their topically-administered compositions may comprise other compounds "...that either do not affect or only minimally affect the activity of the enzyme," it appears that this is a teaching against compounds that have a negative effect on the enzyme. Clearly, it would be desirable to have an active enzyme, thus inclusion of at least one compound which stimulates the activity of AGA would have ensured that such is the case.

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed August 22, 2007, have been fully considered but they are not persuasive. Applicant asserts that the specification provides appropriate written description for AGA activators given the description of test methods in paragraphs [0043] through [0048]. Applicant also asserts that no more than routine experimentation is used to determine whether any given compound stimulates the activity of AGA. However, it is respectfully noted that there is a near infinite number of compounds which can be tested. Thus, extensive experimentation would be required to determine which of the near infinite number of compounds indeed stimulates AGA activity.

With respect to the enablement rejection, the applicant asserts that the Enomaa publication, which was cited as evidence that SDS decreases the activity of AGA, only teaches the decrease of AGA activity at elevated temperatures. It is noted from Figure 3 that temperatures above 60°C result in a significant decrease of AGA activity compared to a sample without SDS. However, it is respectfully pointed out that Figure 3 still shows that for temperatures lower than 60°C (25, 37,42, 50, 56 °C), the activity of AGA is still less than the activity of the corresponding control samples not comprising SDS. Moreover, the cited passage on page 615 and Figure 3 in Enomaa et al. do not show that AGA activity is stimulated by the presence of SDS. Thus, the enablement rejection must be maintained.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re*

Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Though Fein teaches a few hydrolases for the treatment of skin, it would have been obvious to one skilled in the art to substitute hydrolases with other known hydrolases to achieve the predictable result of promoting desquamation. By testing out AGA, the person of ordinary skill in the art would have observed an effect on desquamation. The applicant indicates that US 2004/0115187 shows that only some glycosidases show activity on stratum corneum desquamation whereas similar enzymes (exoglycosidases) have no activity on desquamation. However, it is respectfully noted that US 2004/0115187 states that "...exoglycosidases only very slightly affect desquamation" (page 6, paragraph [0118]). Thus, an effect on desquamation by these enzymes was detected and so US 2004/0115187 does not teach that some of the enzymes tested do not have activity on desquamation, only that the activity varies.

The applicant also asserts that the buffer at a pH of about 6 is not an activator. However, it is respectfully noted that the compounds in the buffer can be considered compounds which stimulate AGA activity when the pH is 6.

In sum, the claims must be rejected over the prior art.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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